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PATENT COOPERATION TREATY

PCT

REC'D 05 FEB 2002

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 99121	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/18012	International filing date *(day/month/year)* 30 June 2000 (30.06.2000)	Priority date *(day/month/year)* 30 June 1999 (30.06.1999)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 33/00, 33/06, 33/14 and US Cl.: 424/663,665,677,678,679,680,681,682,722,723;514/853		
Applicant CORDRAY, SCOTT		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☑ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
08 November 2000 (08.11.2000)	11 January 2002 (11.01.2002)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer John Pak Telephone No. (703) 308-1235

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18012

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed.

☒ the description:
pages 1-7 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages NONE, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages 8-13, filed with the letter of 05 July 2001 (05.07.2001).

☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18012

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	3-6, 9-35	YES
	Claims	1, 2, 7, 8	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1-35	NO
Industrial Applicability (IA)	Claims	1-35	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/18012

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The substitute pages 4, 5, 8-13 are objected description is objected in that PCT rule 11.7 states that the pages are to be numbered in consecutive Arabic numerals. As such, the word "Substitute" should not precede the page numbers.

The substitute pages 4,5,8-13 are objected to under PCT Rule 66.8 as the explanation only indicates that a typographical error was corrected with respect to a decimal point but does not indicate where or what decimal point was corrected.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 5,14,20,35 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claims are not fully supported by the description. The application, as originally filed, did not describe: a range of about 5.0 to about 50.0 grams per liter of aqueous solution.

Claims 5,14,20,35 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: a concentration range was specifically described as being 0.5 to 5 grams per liter and an example was disclosed with 12 grams in 480 cc.

Substitute pages 4,5,8,10,13 are objected under PCT Article 34(2)(b) in that the amendment appears to go beyond the scope of the disclosure as originally filed in that the disclosure only disclose a range of about 0.5 to 5 grams per litre whereas the amendment recites "about 5 to about 50 grams per litre". Although an example is disclosed that has 12 grams in 480 cc, this does not appear sufficient to show that there was a typographical error as to the decimal point. Changing "0.5" to "5" and "5 " to "50" appears to be arbitrary considering that there is no allegedly correct range in the disclosure as originally filed.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. Citations and Explanations:

Claims 3-6, 9-35 meet the criteria set out in PCT Article 33(2), because no single prior art can be found that explicitly discloses a nasal spray formulation comprising a Dead Sea salt and mineral composition which contains a buffer or is present in the amount of 0.5 to about 5 grams per liter of solution.

Claims 1-35 meet the criteria set out in PCT Article 33(4), because the claimed invention finds industrial applicability in the nasal spray art.

Claims 1, 2 lack novelty under PCT Article 33(2) as being anticipated by JP 60164467 A2 (Abstract).
JP 60164467 A2 (Abstract) explicitly discloses a sterile composition comprising Dead Sea salts and water (Abstract).
Examiner has duly considered Applicant's arguments but deems them unpersuasive in that the intended use of a composition does not generally serve to distinguish like compositions and limitations in the preamble are generally not accorded patentable weight.

Claims 7,8 lack novelty under PCT Article 33(2) as being anticipated by EP 0 937 453 A2.
EP 0 937 453 A2 explicitly discloses a sterile composition containing Dead Sea salts (Pg. 3, lines 26-39, Pg. 5, lines 43-60, Pgs. 6-7, Pg. 8, lines 1-15).
Examiner has duly considered Applicant's arguments but deems them unpersuasive in that the intended use of a composition does not generally serve to distinguish like compositions and limitations in the preamble are generally not accorded patentable weight.

Claims 3-35 lack an inventive step under PCT Article 33(3) as being obvious over EP 0 937 453 A2 in view of Gennaro.

EP 0 937 453 A2 discloses a nasal spray formulation containing Dead Sea salts for treatment of nasal or sinus congestion and to soothe coughing irritations due to bronchitis or similar conditions (Pg. 3, lines 26-39, Pg. 8, lines 23, 24).

Gennaro discloses that pharmaceutical preparations are typically sterile, nasal solutions are typically aqueous, isotonic and slightly buffered to maintain a pH of 5.5 to 6.5 and, optionally, contain preservatives and stabilizers, and various aerosol preparations and devices, including methods of producing aerosol in situ (Pgs. 1293, 1500, 1662-1677).

The difference between the prior art and the claimed invention is that the prior art does not explicitly disclose a nasal spray formulation comprising a Dead Sea salt and mineral composition which contains a buffer or is present in the amount of 0.5 to about 5 grams per liter of solution, or a method of treating using a or a method of making a nasal spray containing Dead Sea Salts. However, the prior art amply suggests the same as method of using and method of preparing nasal sprays are well known in the art and it is known to prepare an use a nasal spray containing Dead Sea salts for the treatment of congestion and bronchitis and similar conditions. As such it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

art as above with the expectation of formulating a nasal spray which is effective in obviate the effect of modern environmental conditions on the human body (EP 0 937 453 A2, Pg. 2, lines 24-31).

It is noted that this PCT case claims priority to U.S. Application Serial No. 09/345,043, filed 6/30/99. However, that U.S. Application does not appear to disclose a buffer, pH, amount in grams per liter of aqueous solution, that the product is essentially free of noxious organic impurities, the specific concentration of salts and minerals, a method of treating symptoms of adverse conditions affecting the nasal cavity and passageway comprising the steps of identifying patient with an adverse nasal cavity condition, obtaining a premixed formulation containing a Dead Sea salt and mineral composition in aqueous solution; and administering an aerosol formed from the formulation at least 1 time a day as symptoms of the patient persist, a method of treating symptoms of adverse conditions affecting the nasal cavity and passageway with a Dead Sea salt and mineral composition in aqueous solution, comprising the steps of obtaining a premixed formulation containing a Dead Sea salt and mineral composition in aqueous solution; and self-administering an aerosol formed from said formulations nasally at least 1 time a day as symptoms persist, or a method of producing a nasal spray formulation comprising Dead Sea salt in aqueous solution comprising dissolving Dead Sea salt in aqueous solution and storing this premixed formulation in a container suitable for aerosol nasal administration. As such, although EP 0 937 453 A2 was published after the priority date but before the international filing date, its disclosure is still prior art as to Claims 3-35.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.
Examiner reminds Applicant that the above is based on combination of references not just EP 0 937 453 and that there is no requirement that the claimed invention be explicitly disclosed in any one of the references or that the references contain a working example. Applicant does not appear to have provided any evidence why a skilled artisan would consider the proposed usage minor or of no significance or that the proposed use is "merest wild speculation". Nasal sprays are well known in the art, including saline nasal sprays, as such, it would have been well within the skill of one of ordinary skill in the art to prepare a nasal formulation from Dead Sea salts and one of ordinary skill in the art would expect from the combined teachings of the above references that a composition containing Dead Sea salts would be effective in treating nasal conditions.

---------- NEW CITATIONS ----------

STN/CAS online, file CAPLUS, Acc. No. 1986:18911, Doc. No. 104:18911, (JP 60164467 A2 (ROMAN INDUSTRY CO., LTD., Japan) 27 August 1985), Abstract.

SUMMARY OF THE INVENTION

In accordance with the above and related objects, the present invention provides a nasal spray formulation for use with the treatment of rhinitis, sinusitis, epistaxis, post-surgical irrigation and the like. The nasal spray formulation includes about 1-5% Dead Sea salt or its equivalent. The composition of the Dead Sea salt mixture includes about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide, about 99.4-99.7% chloride. The salt may also include about 0.05-0.2% sulphates, and about 0.5-0.2% insolubles, the latter of which is preferably removed by appropriate filtrations or other means. The salts may comprise about 34-38% water of crystallization. The spray formulation is about 0.5 to about 5.0 grams per liter of aqueous solution. Preferably, the aqueous solution is sterile and contains a buffer, which maintains the pH between 6.5 and 7.5. The spray formulation is preferably also essentially free of noxious organic impurities. "About" in this application means $\pm$ 20%.

Methods for treatment are included in the present invention. In one particular embodiment, the claimed method involves treating symptoms of adverse conditions effecting the nasal cavity and related passageways, which involves identifying a patient with an adverse nasal cavity condition and obtaining a premixed formulation containing a Dead Sea salt or the equivalent formulation and mineral composition in aqueous solution and administering or self-administering an aerosol formed from the formulation at least 1 time a day as symptoms of the patient or individual persist.

A method of producing is also part of the present invention and the formulations which includes dissolving the Dead sea salt in aqueous solution and storing this premixed formulation in a container suitable for nasal aerosol administration.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The present invention relates to a nasal spray formulation used in the treatment of conditions involving the nasal passageway. Specifically, the formulation utilizes the Dead Sea salts to assist in the treatment of rhinitis, sinusitis, epistaxis, and post-surgical irrigation. Rhinitis is the inflamation of the mucous membranes of the nose. Sinusitis is the inflamation of the sinus. Epistaxis is nose bleed or hemorrahage from the nose.

In a preferred embodiment of the present invention, the Dead Sea salt solution comprises about 0.5 to about 5.0 grams per liter of sterile aqueous solution. Said aqueous solution may be or include a buffer, water, or any other pharmacologically acceptable aqueous mixture. The buffer is to maintain the pH between about 6.5 and 7.5. A buffer is Sodium Phosphate, Potassium Phosphate, Sodium Carbonate, or such other as would be used by those skilled in the art to maintain the pH between 6.5 and 7.5. The composition of the Dead Sea salt mixture includes about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide. The halide are preferably about 0.3 -0.6% bromide, 99.4-99.7% chloride, and the mixture may also include about 0.05-0.2% sulphates, about 0.5-0.2% insolubles, the later of which are preferably removed by filtrates. The salts may comprise about 34-38% water of crystallization. The formulation is essentially free of noxious organic impurities, such as human waste, dead marine animals, and fossil fuel spillage. "Essentially Free" is defined as no more than harmless, trace quantities.

Although the preferred embodiment of this invention is the use of Dead Sea salt from the Dead Sea, it is understood that one skilled in the art would be able to artificially create a Dead Sea salt. It is also apparent to anyone skilled in the art, that certain pharmacologically accepted ingredients normally found in nasal spray could be added to the

WHAT IS CLAIMED IS:

1. A nasal spray formulation comprising:

a Dead Sea salt and mineral composition in aqueous solution.

2. The formulation of claim 1 where the aqueous solution is sterile.

3. The formulation of claim 1 defined further as containing a buffer.

4. The formulation of claim 3 where the buffer is to maintain a pH of from about 6.5 to about 7.5.

5. The formulation of claim 1 where the composition is from about 0.5 to about 5 grams per liter of aqueous solution.

6. The formulation of claim 1 where the composition is about 2.5 grams per liter of aqueous solution.

7. The formulation of claim 1 where the composition is essentially free of noxious organic impurities.

8. The formulation of claim 1 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

9. A method of treating symptoms of adverse conditions affecting the nasal cavity and passageway, the method comprising the steps of identifying patient with an adverse nasal cavity conditions;

a. obtaining a premixed formulation containing a Dead Sea salt and mineral composition in aqueous solution; and

b. administering an aerosol formed from the formulation at least 1 time a day as symptoms of the patient persist.

10. The method of claim 9 wherein said conditions include rhinitis, sinusitis, epistaxis and post-surgical irritation.

11. The method of claim 9 wherein said Dead Sea salt and mineral composition is in sterile aqueous solution.

12. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution contains a buffer.

13. The method of claim 12 wherein the buffer is to maintain a pH from about 6.5 to about 7.5.

14. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution is from about 0.5 to about 5 grams of salt per liter of said aqueous solution.

15. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution is about 2.5 grams of salt per liter of said aqueous solution.

16. The method of claim 9 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

17. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution is essentially free of organic impurities.

18. A method for treating symptoms of adverse conditions of the nasal cavity and passageway with a Dead Sea salt and mineral composition in aqueous solution, the method comprising the steps of obtaining a premixed formulation containing a Dead Sea salt mineral composition in aqueous solution; and self administering an aerosol formed from said formulations nasally at least 1 time a day as symptoms persist.

19. The method for claim 18 wherein said conditions include rhinitis, sinusitis, epistaxis and post-surgical irritation.

20. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution is from about 0.5 to about 5 grams per liter of said aqueous solution.

21. The method of claim 18 wherein a Dead Sea salt mineral composition is in sterile aqueous solution.

22. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution contains a buffer.

23. The method of claim 22 wherein the buffer is to maintain a pH of from about 6.5 to about 7.5.

24. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution is about 2.5 grams per liter of said aqueous solution.

25. The method of claim 18 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

26. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution is essentially free of noxious, organic impurities.

27. A method of producing a nasal spray formulation comprising Dead Sea salt in aqueous solution, the method comprising dissolving Dead Sea salt in aqueous solution and storing this premixed formulation in a container suitable for aerosol nasal administration.

28. The method of claim 27 wherein a Dead Sea salt mineral composition in aqueous

solution is from about 0.5 to about 5 grams per liter of said aqueous solution.

29. The method of claim 27 wherein Dead Sea salt mineral composition in aqueous solution is about 2.5 grams per liter of said aqueous solution.

30. The method of claim 27 wherein Dead Sea salt mineral composition is in sterile aqueous solution.

31. The method of claim 27 wherein Dead Sea salt mineral composition in sterile aqueous solution contains a buffer.

32. The method of claim 31 wherein the buffer is to maintain a pH of from about 6.5 to about 7.5.

33. The method of claim 27 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, and halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

34. The method of claim 27 wherein a Dead Sea salt mineral composition in aqueous solution is essentially free of noxious, organic impurities.

35. A nasal spray formulation comprising a Dead Sea salt and mineral composition having about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8%

sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride, where said Dead Sea salt and mineral composition contains a buffer maintaining a pH from about 6.5 to 7.5 and is from about 0.5 to about 5 grams per liter of sterile aqueous solution and is essentially free of noxious, organic impurities.